REMARKS

Applicant wishes to thank the Examiner for the courtesy extended in granting a telephone interview which was held on August 30, 2007, followed-up by a second telephone interview held on September 13, 2007, discussing the relevance of the cited reference Cha et al (USP 5,702,717) to the subject invention and in particular to claim 1.

Claim 1 has been amended as discussed with the Examiner to clearly overcome the broad reading of the original wording of claim 1 on the Cha et al reference.

It should further be noted that the Cha et al reference does not disclose nor suggest a ratio z/y equal to 1.

The rejection of claims 1-7 and 12-15 under 35 USC 102(b) as being anticipated by Cha et al '717 is respectfully traversed.

The present invention, is directed specifically to amphiphilic block copolymeric micelles containing a small quantity of functional groups in its hydrophobic block. This is now more clearly defined in claim 1 as amended and in pending claims 2-7 and 12-15. Claim 1 now recites a micelle composition for drug delivery comprising an amphiphilic block copolymer having at least one hydrophilic blocks(A) and at least one hydrophobic blocks(B) wherein at least one repeating unit

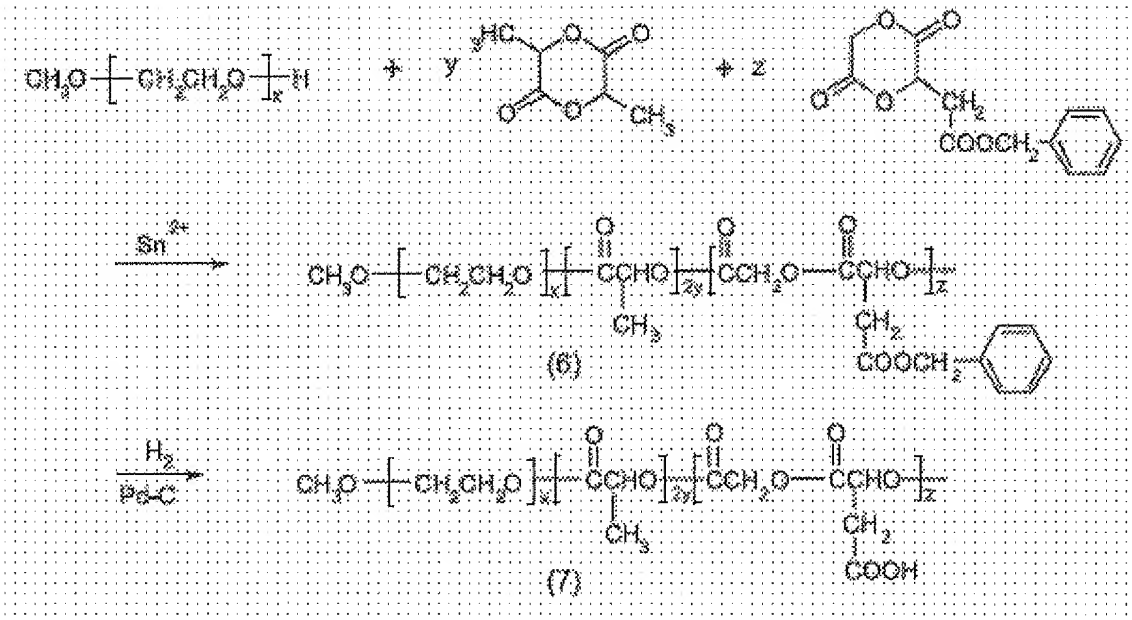
of said hydrophobic block of said amphiphilic block copolymer includes active hydrogen-containing functional groups is selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups, and wherein (z) represents the repeating units of the hydrophobic block carrying said functional groups and is in a range of 1.1 to 30, and wherein (y) represents the number of repeating units of hydrophobic block not containing the functional group and (y) is correlated to (z) such that a ratio, z/y, is in the range of 0.015 to 2. 30.

By way of review, Cha '717 teaches a system and method for parenteral delivery of hydrophilic drugs, highly water-soluble peptide and protein drugs, in particular (see col. 6, lines 31-34), encased in a biodegradable block copolymer in a liquid composition, wherein the biodegradable block copolymer comprises a hydrophobic A polymer block comprising a member selected from the group consisting of poly(α-hydroxy acids) and poly(ethylene carbonates), and a hydrophilic B polymer block comprising polyethylene glycol units.

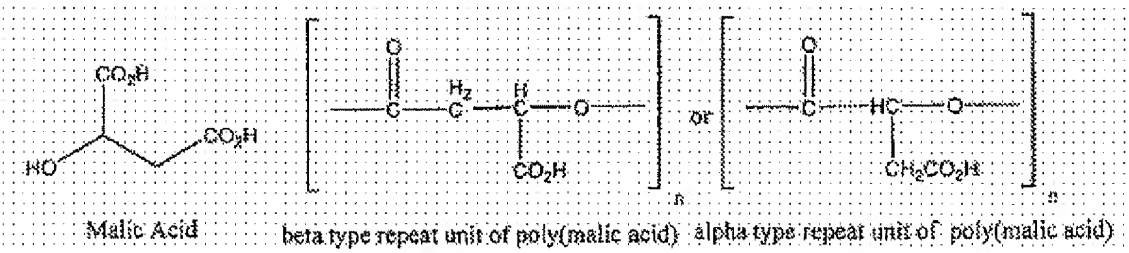
The drug delivery system of Cha '717 is designed to administer a hydrophilic drug, particularly a highly water-soluble peptide and protein drug. On the other hand, the drug delivery system of the present invention is to administer a hydrophobic drug by incorporating the drug in the hydrophobic core of the specified micelle composition having an enhanced drug-loading capacity and sustained-release characteristics.

The technical feature of the present invention is a micelle composition comprising an amphiphilic block copolymer carrying an active hydrogen-containing functional group selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups, which enhance the core's affinity to a hydrophobic drug. The term "active hydrogen-containing" is used herein instead of "hydrogenated" to better clarify the nature of said functional group. Such a group is capable of enhancing the affinity between the hydrophobic core and the hydrophobic drug, through, e.g., hydrogen bonding.

Further, in the method of the present invention, the active hydrogen-containing functional groups are introduced to the hydrophobic block chain of the copolymer by: a) subjecting a functional monomer (e.g., 3-{(benzyloxycarbonyl)methyl}-1,4-dioxane-2,5-dione) to copolymerization with hydrophobic and hydrophilic blocks to obtain an amphiphilic block copolymer, wherein the hydrophobic block comprises benzyl groups, and b) subjecting the copolymer to hydro-debenzylation by hydrogenolysis using hydrogen in the presence of a catalyst (see page 5, lines 6-19, and scheme 2 of Exhibition 1). Namely, as shown below, in the present invention, a specified number of said functional groups can be introduced to the hydrophobic block chain of the copolymer by controlling the z/y ratio.



Whereas, the Examiner has pointed out that Cha '717 teaches that the hydrophobic block can comprise malic acid, which may convert to an active hydrogen-containing functional group when subjected to polymerization as described below:



However, putting aside the fact the self-polymerization of malic acid monomers does not easily occur, even if the malic acid is polymerized, each repeating unit of poly(malic acid) would have one carboxylate functional group. That is, the imaginary malic acid polymerized block of Cha '717 would have too many functional groups and would not satisfy the specified z/y ratio of the present invention.

Accordingly, Cha '717 clearly fails to teach the inventive micelle composition for drug delivery comprising an amphiphilic block copolymer.

Accordingly, it is believed that the present invention is novel over Cha '717.

The Examiner has rejected claims 1-15, and claims 1-7 and 12-15 under 35 U.S.C. § 103(a) as being unpatentable over Cha '717 and Seo et al. (WO 01/87345; hereinafter, referred to as Seo '345). However, applicants respectfully traverses the rejection for the reasons provided below.

As mentioned above, Cha '717 teaches a system and method for parenteral delivery of hydrophilic drugs, highly water-soluble peptide and protein drugs, in particular (see col. 6, lines 31-34), encased in a biodegradable block copolymer in a liquid composition, wherein the biodegradable block copolymer comprises a hydrophobic A polymer block comprising a member selected from the

group consisting of poly(α-hydroxy acids) and poly(ethylene carbonates), and a hydrophilic B polymer block comprising a polyethylene glycol.

Seo '345, on the other hand, discloses a composition capable of forming a polymeric micelle in a body fluid or in an aqueous medium, said composition comprising an amphiphilic block copolymer having a hydrophilic A block component and a hydrophobic biodegradable B block component, wherein the biodegradable B block component of the copolymer has a modified end group having affinity to a hydrophobic drug.

As discussed above, the present invention is different from Cha '717 in that the block copolymer carries a specified number of active hydrogen-containing functional groups in the hydrophobic block chain of the copolymer to effectively enhance the interaction of a hydrophobic drug with the hydrophobic block of the copolymer. Further, as discussed below, the inventive micelle composition and pharmaceutical composition show unexpectedly advantageous effects arising from the above feature of the block copolymer.

Accordingly, the inventive micelle composition of claim 1 and the pharmaceutical composition comprising same of claim 12 are patentable over Cha '717, and all claims depending from claims 1 and 12 of the present invention are also patentable over Cha '717.

The Examiner has pointed out that Seo '345 discloses several hydrophobic polymers that have functional groups that remain after the monomers were polymerized (e.g., poly(amino acid)).

However, polymerization of the amino acid monomer does not easily occur, and even if such polymerization takes place, some provide no active hydrogen-containing functional group, while others, too many active hydrogen-containing functional groups per repeating unit. Therefore, Seo '345 cannot offer the number of active hydrogen-containing functional groups in its hydrophobic block specified in the present invention.

In contrast, the inventive drug delivery system comprises an amphiphilic block copolymer, wherein the block copolymer carries a controlled number of functional groups (z), i.e., 1.1 to 30 active hydrogen-containing functional groups, in the hydrophobic block chain of the copolymer, and the z/y ratio is in the range of 0.015 to 2, y being the number of other repeating units in the hydrophobic block.

Accordingly, Seo '345 clearly fails to render obvious the inventive micelle composition, and a pharmaceutical composition comprising a hydrophobic drug introduced in the hydrophobic block of the micelle composition.

Owing to the functional group having active hydrogen-containing groups incorporated in the hydrophobic block, the inventive pharmaceutical

composition has a markedly enhanced drug content, a prolonged drug release time, and a markedly reduced degradability of the micelle as compared with a pharmaceutical composition comprising the micelle composition of Cha '717 or Seo '345, which has less than 1.1 or more than 30 functional groups in each of the hydrophobic block of the copolymer.

Specifically, as can be seen in the following Table, which is based on the data of Tables 1 and 2 in the specification of the present application, the inventive compositions contained a higher amount of the drug in the hydrophobic core than that of the Comparative Example 1, which corresponds to Cha '717 or Seo '345, and showed a longer drug release time and a shorter degradation time of the micelle as compared with Cha '717 or Seo '345.

Further, as more functional groups are introduced into the hydrophobic block, the drug release time becomes longer. Further, as the number of carboxyl groups introduced into the hydrophobic block increased, the micelle degradation time became shorter. Accordingly, a micelle composition having more than an adequate number of functional groups rapidly degrades after releasing the drug.

In contrast, if the block copolymer contained more than the specified number of carboxyl groups (more than 30, see Comparative Example 2), it fails to form a micelle, and thus, such copolymer is not suitable for drug delivery.

		Number of functional groups of the copolymer	Saturation drug content (wt%)	Drug release time (hr)	Degradation time of the micelle (day)
Present invention	Example 1	1.34	8.0	21	10
	Example 2	2.78	13.7	40	7
	Example 3	3.74	14.9	52	6
	Example 4	11.5	16.9	59	5
	Example 5	23.0	16.8	60	4
Comparative Example 1		**0**	**3.8**	**8**	**20**
Comparative Example 2		**30.3**	-	-	-

Accordingly, the inventive micelle composition comprising 1.1 to 30 functional groups in the hydrophobic block of the amphiphilic copolymer can carry a large amount of a hydrophobic drug, and exhibit satisfactory sustained-release characteristics.

It is believed that the technical constitution and effect according to the present invention are not obvious over Cha '717 and Seo '345, and therefore, the rejection under 35 USC 103 should be withdrawn.

CONCLUSION

In view of the foregoing discussions, it is respectfully submitted that the present invention as defined in the pending claims 1 to 15 should be allowed in their present form.

Respectfully submitted
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CERTIFICATE OF TRANSMISSION

I hereby certify that this Amendment w/RCE is being submitted to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via EFS-Web on September 28, 2007.

Audrey de Souza